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To smell the SLE-CNS involvement

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Central Nervous System involvement in Systemic Lupus Erythematosus (**CNS-SLE**) is very common and ranges between 20% – 70% of the patients. The CNS involvement is listed in the ARA criteria for SLE diagnosis.

CNS-SLE is associated with more than 20 different autoantibodies (1). Yet, remarkable among them are the **anti-P-ribosomal antibodies** (anti-PR) (2). These autoantibodies directed mainly against the carboxy 22 amino acids of the PO, P1 P2 ribosomal phosphoproteins. They are capable of penetrating lived cells and inducing apoptotic changes as well as leading to inhibition of specific cytokine secretion (3-5). The titer of the autoantibodies correlates with disease activity, kidney involvement and hepatitis (6-8).

Anti-PR were first reported to associate and correlate with CNS-SLE and especially psychosis in 1987(9). Subsequent analyses could only partially repeat Bonfa's conclusions (2-3). The contradictory results may stem from technical discrepancies (2-3), multiplicity of autoantibodies causing CNS-SLE (1,10), and differences in the time of drawing the blood in relation to the time when the patient had the CNS involvement.

We employed affinity purified anti-PR on a PR column and injected them directly into the brain ventricles of Balb/c mice. Irrelevant Igs were employed as controls. The analyses entailed a variety of neurological tests known to evaluate cognitive impairment, anxiety states, depressive conditions and motor competence of the mice.

Mice injected with anti-PR clearly expressed **depressive behavior**, characterized mainly by floating pattern rather than swimming in an enforced swimming tests. These floating pattern could be reversed by a specific therapy with monoclonal anti-idiotypic antibody to anti-PR (11), by IVIG as well as Fluoxetine (Prozac) an anti-depression drug. No response was achieved with anti-psychotic drug. The control mice were not affected in their behavior following the injection of the irrelevant Ig (12).

The human purified anti-P-R, were shown to bind to CNS structures consisting with the **smell apparatus** (i.e. amygdale, hypocampus and other parts of the limbic systems).

Smell defects characterize bulbectomized (cutting the olfactory nerves) depressive mice (13), as well as depressive women (14). Such depression can be overcome by exposing mice and

humans to citrus fragrance (15).

Our studies show for the first time the active induction of a psychiatric condition (i.e. depression) with a specific autoantibody, i.e. **anti-PR** (16). Furthermore, the results allude to a novel mechanism to explain the induction of CNS-SLE depression (i.e. involvement of the smell apparatus).

These data may pave the road to a novel approach to depression in CNS-SLE and its therapy as well as in other CNS conditions (12,17,18-21).

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